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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis, biological activity and docking study of some new isatin Schiff base derivatives

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Abstract A set of novel Schiff bases of isatin were synthesized and characterized by reaction of isatin with various aromatic or heterocyclic primary amines. Cytotoxic activities for some of the synthesized compounds were evaluated by MTT assay in three human cancer cell lines (HeLa, LS180 and Raji). Half of the tested compounds showed good cytotoxicity in HeLa cells. 3-(2-(4-nitrophenyl) hydrazono) indolin-2-one was found to be the most potent molecule among the studied isatin derivatives. Docking studies of 3-substituted indolin-2-one scaffolds on vascular endothelial growth factor receptor 2 (VEGFR-2) involved in cell proliferation and angiogenesis was performed. 3-(naphthalen-1-ylimino) indolin-2-one and 3-(2-(4-nitrophenyl) hydrazono) indolin-2-one exhibited higher docking binding energies with receptor. For 3-(2-(4-nitrophenyl) hydrazono) indolin-2-one, H-bond interaction with Cys917 residue of target active site was in common with reported crystallographic benzoimidazole derivative (PDB code: 2OH4). New key H-bonds involving Glu915, Asn921, and Arg1049 residues in VEGFR-2 active site could be detected for 3-(2-(4-nitrophenyl) hydrazono) indolin-2-one. Extended lipophilic rings containing H-bond acceptors on the 3 position of indoline scaffold seemed to be important factors in developing potent VEGFR-2 inhibitors virtually. Based on the ligand efficiency indices, some isoxazole or thiazole substituted isatin derivatives may be regarded as efficient candidates for further molecular developments of anticancer agents.

Keywords Isatin · Schiff base · Synthesis · Cytotoxicity · Docking

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Introduction

Isatin is an endogenous compound isolated in 1988 (Glover *et al.*, 1988) and reported to possess a wide range of central nervous system activities (d'Ischia *et al.*, 1988; Varma and Nobles, 1975). It has also been found as a metabolic derivative of adrenaline in humans (d'Ischia *et al.*, 1988). Isatin is a natural product found in a number of plants including those of the genus isatis and also has been found as a metabolic derivative of humans (d'Ischia *et al.*, 1988). Various derivatives of isatin are known to possess a wide range of pharmacological properties (Varma and Nobles, 1975; Varma and Khank, 1977). Among the important pharmacological effects, antibacterial (Pandeya *et al.*, 2000, 1999a; Sarangapani and Reddy, 1994; Varma and Nobles, 1975; Sridhar *et al.*, 2001), antifungal (Pandeya *et al.*, 2000; Pandeya *et al.*, 1999), antiviral (Varma and Nobles, 1967; Singh *et al.*, 1983; Logan *et al.*, 1975), and anti-HIV (Pandeya *et al.*, 1999b; Pandeya *et al.*, 2000) activities are worth noting. Within the context of enzyme inhibitors, isatins (also known as 2,3-dioxindoles) have seen recent applications in the inhibition of cysteine and serine proteases (Iyer and Hanna, 1995; Webber *et al.*,